PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Complementary and alternative asthma treatments and their association with asthma control: a population-based study
AUTHORS	Chen, Wenjia; FitzGerald, J Mark; Rousseau, Roxanne; Lynd, Larry; Tan, Wan; Sadatsafavi, Mohsen

VERSION 1 - REVIEW

REVIEWER	edzard Ernst emeritus professor university of Exeter uk no conflicts of interest to declare
REVIEW RETURNED	12-Jun-2013

GENERAL COMMENTS	this is a well-planned, well-executed, and well-written paper with important and clear findings which are carefully and critically discussed. I have no major or minor criticisms

REVIEWER	Dr Matthew Masoli Consultant Respiratory Physician Plymouth Hospitals NHS Trust, UK No competing interests
REVIEW RETURNED	09-Jul-2013

GENERAL COMMENTS	This is an interesting study, well written and of interest to health professionals. The obvious limitations have been described within the paper in particular the use of self reported prescription medication chart. Interestingly 42% of individuals were uncontrolled with 42% having low (PDC<50%) intake of controller medications. Uncontrolled asthma was associated with increased CAM use although it is important to note that most of the CAM use was with breathing exercises, herbal medicines and vitamins. There does not appear to be any evidence that adherence with controller medications is lower in the CAM users. CAM users had lower FEV1 (almost statitically significant p=0.06)and there was similar controller intake. If anything higher in the CAM users. this should be discussed. Do the CAM users have more severe asthma, hence are more symptomatic and therefore looking for additional treatments to improve their symptoms. It's interesting that breathing exercises was the most frequent CAM as this is increasingly becoming part of the systematic management of difficult / severe asthma.

VERSION 1 – AUTHOR RESPONSE

Reviewer: edzard Ernst
emeritus professor
university of Exeter
uk
no conflicts of interest to declare

this is a well-planned, well-executed, and well-written paper with important and clear findings which are carefully and critically discussed. I have no major or minor criticisms
[Response: this comment does not require a response. We thank the reviewer for these kind comments.]

Reviewer: Dr Matthew Masoli
Consultant Respiratory Physician
Plymouth Hospitals NHS Trust, UK

No competing interests

This is an interesting study, well written and of interest to health professionals. The obvious limitations have been described within the paper in particular the use of self reported prescription medication chart. Interestingly 42% of individuals were uncontrolled with 42% having low (PDC<50%) intake of controller medications.
[Response: this comment does not require a response. We thank the reviewer for insightful comments on our paper].

Uncontrolled asthma was associated with increased CAM use although it is important to note that most of the CAM use was with breathing exercises, herbal medicines and vitamins. There does not appear to be any evidence that adherence with controller medications is lower in the CAM users. CAM users had lower FEV1 (almost statitically significant p=0.06) and there was similar controller intake.
[Response: this comment does not require a response].
If anything higher in the CAM users. this should be discussed. Do the CAM users have more severe asthma, hence are more symptomatic and therefore looking for additional treatments to improve their symptoms.
[Response: Our primary objective of studying the association between asthma control (instead of severity) and CAM use was in line with the modern guidelines which emphasize asthma control over asthma severity. In addition, as the reviewer is well aware of, in a cohort of patients who receive different doses of controller and rescue treatment, it is difficult to measure the innate level of asthma severity (which is masked and blurred by treatment). We were worried that individual's innate level of activity (which can be called asthma severity) might be a confounding variable (e.g., severe cases are more likely to use CAM, and are more likely to be uncontrolled, causing a spurious association between lack of control and CAM use, as the reviewer mentioned). However, upon considering the following three factors, we decided not to further adjust for severity:
- Adjusting for controller medication use (in term of the proportion of days covered) does, to a large extent, capture the confounding effect of innate activity (e.g., patients who are uncontrolled despite PDC of 85% have more severe asthma than those who are controlled with a PDC of 30%) on the relation between CAM use and asthma control. We argue that within strata of controller therapy use (i.e., patients with the same level of PDC) and asthma control level, innate asthma activity is most likely similar. So indeed we have adjusted for asthma severity through intensity of controller use and current level of control.
- Many indicators of asthma severity are also used in the definition of control (e.g., FEV1, daily impairment, etc.). Adjusting for such measures of asthma severity would introduce a diluting bias in the association of control and CAM use due to collinear effects. This is not a limitation of our study: asthma control and severity are correlated anyways and any non-randomized study will face the same

issue.
- We are not claiming uncontrolled asthma causes CAM use (for which asthma severity can be a confounder). We are reporting on 'association', and its clinical and policy relevance (i.e., use of CAMs might be an 'indicator' of uncontrolled asthma).
We hope that the above lines of reasoning has satisfied the reviewer that we really could not have discerned, yet controlled for, the innate level of asthma severity over and above controller medication use. However, upon considering the reviewer's comments we have decided to mention the potential role of asthma severity in the observed association. Accordingly we have added the following sentences to the end of the first paragraph of the Discussion:
"Our study therefore suggests that the use of CAMs in patients with asthma is high, and is associated with worse asthma control. In addition, we found breathing exercise, a modality often used by patients with more severe asthma, to be the most common type of CAM. This, combined with a lower baseline FEV1 (P=0.06) among CAM users compared with non-users, might indicate that CAM users tended to have more severe asthma."]
It's interesting that breathing exercises was the most frequent CAM as this is increasingly becoming part of the systematic management of difficult / severe asthma.
[RESPONSE: Agreed. We think the high prevalence of breathing exercise is an interesting finding and we have now highlighted this in the discussion (see the response to your previous comment).]